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Rocco S Barrese
Dilworth & Barrese
333 Earle Ovington Boulevard
Uniondale, NY 11553

EXAMINER	
KINGAN, TIMOTHY G	

ART UNIT	PAPER NUMBER
1797	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,501	GAUER, CHRISTOPH	
	Examiner	Art Unit	
	TIMOTHY G. KINGAN	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/28/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. Applicant's arguments filed 04/11/2008 have been fully considered but they are not persuasive. Wixforth teaches separation of a smaller portion of liquid (rather than movement of the entire drop) from the reservoir by selection of the strength of the surface wave ([0077]). Wixforth teaches movement and separation of drops for analysis [0014] and that two drops may be moved and mixed for reaction [0041], a fundamental form of titration comprising mixing of one drop with another. It would have been obvious to one of ordinary skill in the art, from the teaching of Wixforth on separation of drops from a reservoir and the mixing of two drops for reaction, to use simple repetition of surface wave application for movement of multiple smaller portions in order to achieve a step-wise reaction (titration comprises division of a reaction by mixing in one or more steps) of titrant with analyte. No further level of control of drop size, with respect to volume or precision in repetition, is claimed by applicant. The essential elements of the instant application, use of surface tension for holding a drop of titrant or analyte together, use of surface acoustic waves to move a drop or first separate and then move a portion thereof, as well as movement along a path defined by surface wetting properties and combination/mixing with a second drop, are all taught or suggested by Wixforth. Wixforth teaches that the strength of the surface wave needed can be determined in a simple preliminary experiment ([0077]), providing suggestion for experimentation in control of the size of the separated drop by manipulation of the strength of the wave. The combined Wixforth teachings that a drop can be confined by

manipulating the surface wetting properties and that multiple drops of liquid can be moved ([0012]) provides suggestion for use of the titrant drop (apart from the pathways, **15**, Fig. 1) as a source of smaller drops in a titration. Further, it would have been obvious to one of ordinary skill in the art to use the combined teachings of Wixforth in arriving at the suggestion that the relative sizes (volumes) of the smaller portion of titrant and the analyte receiving the titrant can be controlled by appropriate sizing of the reservoir and analyte drops together with the selected surface wave separating the smaller portion.

With regard to Claim 11, wherein the reservoir drop is moved over a region that is more strongly wetted than the surrounding region, it is noted that the prior art teaches that the substrate outside the path is “surrounding region” that is not wetted; thus it may have been applicant’s intention to indicate that a portion of the path of the drop, **3**, the direction of which may be determined by the directionality of the surface wave (separately from the surface wetting properties) as taught by the prior art (Wixforth [0097]), has different wetting properties than the remaining path of the drop, exclusive of remaining substrate. As written, the prior art elements suggest the limitation of the claim, in that surface wave alone may determine the direction of the drop, and the surface can be imparted with different wetting properties, providing means to generate small drops when the reservoir drop moves across a hydrophobic surface and crosses a hydrophilic surface.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 10/501501, filed on 12/28/2001.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over A. Wixforth, U.S. Patent Application Publication 2001/0055529 (herein after Wixforth). For Claim 1, Wixforth teaches moving individual drops of a liquid forward [0012] and that two drops of liquid can be moved toward each other for mixing and purposes of a reaction (titration). Wixforth teaches application of a liquid on the chip 2 ([0075] and Fig.

1) (flat surface). Wixforth also teaches that drops of liquid being transported do not run away from each other (are held together) because of surface tension [0012]. Wixforth teaches movement of both drops toward each other [0041] but is silent on movement of titrant to fixed analyte. It would have been obvious to one of ordinary skill in the art, from the teachings of Wixforth on movement of drops along a path defined by wetting properties, to move a single drop (of titrant) toward a fixed second drop (of analyte) in order to affect a reaction, since such single drop movement would require fewer transducers on the substrate for moving liquid drops.

Wixforth is silent on the relative sizes of drops of titrant and analyte drops. Wixforth teaches small drop-shaped quantities of liquid (titrant) separated and transported from the rest of the volume to reservoir 13 where it comes in contact with a quantity of analyte ([0077] and Fig. 1) for reaction (p. 9, Claim 25). It would have been obvious to one of ordinary skill in the art to use quantities of titrant smaller than that of analyte in order to achieve a total reaction volume within the limits of the small spaces of surfaces defined by their wetting properties.

Wixforth teaches the use of analysis stations on the chip surface in which matter interacts with a measurement quantity, such as illumination, for measurement [0014] with respect to a physical, chemical or biological characteristic [0044]. It would have been obvious to one of ordinary skill in the art to use additional pulses of surface waves for separating drops of titrant in order to achieve the flexibility of reaction volumes associated with both amplitude of acoustic wave and the drop size that can be achieved by such waves limited by the properties of the electrodes and the solid-body surface.

For Claim 2, Wixforth teaches use of surface acoustic waves sent to at least one quantity of matter (analyte drop) for mixing (p. 9, Claim 27), after at least two quantities of material are brought into contact (p. 9, Claim 25 and [0054], [0082]).

For Claim 3, Wixforth teaches the process of moving at least two quantities of matter into contact on the solid-body surface, thus moving one quantity (titrant) towards the other quantity (analyte) [0054].

For Claim 4, Wixforth teaches bringing a quantity of liquid to the chip [0075], at least part of which is to be used as a reservoir for matter (titrant) (p. 10, Claims 46-47) that can be set in motion (is held together) because of surface tension [0076]. Wixforth further teaches that one quantity of the liquid can be separated from the rest [0039], [0046], [0077] and such liquid can be set in motion and moved forward [0047]. From this and the additional teaching of Wixforth that drops can be moved to bring them into contact in this way, it would have been obvious to one of ordinary skill in the art to use such separation and movement to move a drop of titrant separated from a reservoir in order to bring it into contact with a second drop of liquid [0041] (analyte) in order to divide a reaction between drops into multiple steps, a method of configuring a reaction that is well known in the art to achieve finer resolution in determination of concentrations of reactants.

For Claim 5, Wixforth teaches movement of individual drops (titration quantities) forward [0012] in response to surface waves [0013], and such movement results from the impulse transfer of the surface wave or waves to drops [0006], [0019].

For Claim 6, Wixforth teaches one or more interdigital transducers [0028] that may be used on a piezoelectric substrate (solid surface) [0030], [0048], and that such transducers are used to generate surface acoustic waves [0028] with a direction of emission perpendicular to the axis of the transducer [0028] which can be arranged for waves in the direction of the desired momentum transfer (Figs. 1-5).

For Claim 7, Wixforth teaches bringing a quantity of liquids (analyte) to one or more reservoirs of the chip ([0075], [0077[) and that the chip's surface or parts or regions (analysis point) of the surface may be modulated in wetting properties by coating to define hydrophobic and hydrophilic regions [0021]. Wixforth teaches that such regions [0072] (analysis point) may be hydrophilic with respect to surrounding region [0071] and will therefore be more strongly wetted.

For Claim 8, Wixforth teaches that a quantity of liquid may be reversibly immobilized (anchored) on the surface of the solid by appropriate functionalization such as imparting different wetting properties than the surrounding surface [0053], such as by defining hydrophobic and hydrophilic regions according to Claim 7 above [0021]. Further, Wixforth teaches that reservoir regions 11 (Fig. 1) are more hydrophilic [0071] than the surrounding region so that matter (reservoir drop) preferentially stays in this region [0072] since it is more strongly wetted than more the hydrophobic surrounding region.

For Claim 9, Wixforth teaches application of liquid sample on the chip 2 [0075] (solid surface), that one quantity of the liquid (titrant) can be separated from the rest ([0046] and [0077]) (reservoir) and that such titrant can be guided from a reservoir on a

conducting path formed by surface modulation of wetting properties [0021] to bring it into contact with a reservoir [0077]. Wixforth teaches movement of two drops toward each other [0041] but is silent on movement of titrant to fixed analyte. It would have been obvious to one of ordinary skill in the art to move a single drop toward a fixed second drop in order to affect a reaction, since such single drop movement would require fewer transducers on the substrate for moving liquid drops.

For Claim 10, Wixforth teaches that one quantity of the liquid (titrant) can be separated from the rest [0046] (reservoir drop), and that such titrant can be guided from a reservoir on a conducting path [0021] to a receiving reservoir [0072] (anchor point) or an analysis point ([0085], Figs. 1-3). Wixforth is silent on the width of the connection region. Wixforth teaches that, while conducting paths for liquid transport [0020] can be defined in their breadth [0021], movement of matter (reservoir drop) (off anchor points 11 and 13 (Fig. 1)) is caused by surface waves [0006]. Therefore, it would have been obvious to one of ordinary skill in the art to make such conducting paths 15 (Fig. 1) sufficiently narrow to prevent a drop from leaving the anchor point in the absence of an external force, the same physical property of the surface with respect to wetting properties that prevents movement of a drop in any direction away from an anchor point.

For Claim 11, Wixforth teaches that a drop can be moved intact on a path from one reservoir to another defined by surface-wetting properties [0075] (is more strongly wetted by liquid) and that such path is smaller in contact area than that of the reservoir drop (Figs. 1-3). Wixforth also teaches that direction of such drops can be changed by

an appropriately positioned transducer [0084], from a supply reservoir to a receiving reservoir. Wixforth teaches that conducting paths can be functionalized, using a number of alternative technologies [0049], to modulate the wetting properties of paths with respect to surrounding surface [0021]. In addition, Wixforth teaches that a drop may be moved based on the directionality of the surface wave, apart from preparation of the surface [0097]. Wixforth is silent on use of a region on the surface, 41, to separate a titration quantity. It would have been obvious to one of ordinary skill in the art to use the directionality of drop in response to surface wave alone and the ability to impart different wetting properties to regions of the surface in order to generate smaller drops on the path of the reservoir drop. One of ordinary skill in the art would have found desirable to use such differential wetting of the path in the device of Wixforth in order to provide a separate physical mechanism for generating drops that may increase the range of drop size by exploiting the ability to control surface properties, separate from surface wave frequency or amplitude.

For Claim 12, Wixforth is silent on use of a climatic chamber. It would have been obvious to one of ordinary skill in the art to use a climatic control chamber in order to maintain volume and prevent drying from the boundaries of very small drops of liquid during and after the time of application of such drops, their movement on the substrate and their interaction with each other for purposes of measuring a reaction.

For Claim 13, Wixforth teaches launching a surface acoustic wave in the direction of an analysis point [0085]. Further, Wixforth teaches matter can be irradiated with a surface wave for the purpose of studying the effect on the surface acoustic wave

[0051]. Wixforth is silent on the period of such study, during and/or after the reaction, and on parameters of the wave. It would have been obvious to one of ordinary skill in the art to use such surface wave, for studying effects throughout and after the reaction in order to obtain data reflecting kinetic properties of the reaction, and that such study on acoustic waves would require choice of parameters of the wave to measure; implicit in such study is measurement of change in a specific property of the wave.

For Claim 14, Wixforth teaches the analysis of matter within at least one region on the surface for at least one physical, chemical or biological characteristic (p.9, Claim 19). It would have been obvious to one of ordinary skill in the art that reaction heat is one such physical property, since the free energy of a chemical reaction includes an enthalpic component, that of giving off to or absorbing heat from its surroundings.

For Claim 15, Wixforth teaches the analysis of matter within at least one region on the surface for electric properties (p. 9, Claim 21). It would have been obvious to one of ordinary skill in the art that electrical conductivity is one such electric property, since ability to complete an electric circuit deriving from charged analytes in solution forms the basis for such conductivity.

For Claim 16, Wixforth teaches the analysis of matter within at least one region on the surface for at least one property, including optical (p. 9, Claim. 21). It would have been obvious to one of ordinary skill in the art that color change is one such optical property, since such change is based in the absorption/transmission properties of light with respect to wavelength that is measured with optical detectors or by eye.

For Claim 17, Wixforth teaches the analysis of matter within at least one region on the surface for at least one physical, chemical or biological characteristic (p.9, Claim 19). It would have been obvious to one of ordinary skill in the art that pH is one such chemical property, since pH is a numerical parameter representing concentration of acid (a chemical) in solution.

For Claims 18-20, Wixforth teaches that an interdigital transducer may be operated to generate acoustic surface waves, according to an inverse piezoelectric effect, spreading perpendicular to the axis of the transducer [0028]. Wixforth further teaches that such piezoelectric effect can be generated in a substrate if a piezoelectric substrate is used [0030], and that the direction of emission of such waves is controlled by orientating the transducers on the substrate for desired momentum transfer (Figs. 1-4).

For Claim 21, Wixforth teaches separating a small drop from the matter in region **5** (Fig. 1). Wixforth does not teach a constriction between the anchor point and path (Fig. 1, **11** and **15**, respectively, of Wixforth). It would have been obvious to one of ordinary skill in the art at the time of invention to use a constriction narrower at the anchor point in extending use of the physical principles of surface tension and wetting properties of the solid-body surface, in order to maintain a minimum volume of source titrant to reduce the possibility of drying in the extension region of the source, **5,** but to allow facilitated movement of separated drops, that pass the constriction, along a defined path according to the teachings of Wixforth.

Wixforth teaches one or more interdigital transducers to generate surface acoustic waves [0028] (generate external force) to move drops away from the reservoir [0077]. Wixforth does not teach movement of such drops towards an analyte drop, but does teach movement toward an analysis reservoir, 13 [0075]. Further, Wixforth teaches movement of drops from separate reservoirs to a mixing region to affect mixing [0081] (reaction). It would have been obvious to one of ordinary skill in the art to use such analysis regions with analyte to affect reaction between titrant and analyte by movement of titrant toward analyte, as an alternative to movement of both titrant and analyte, in order to reduce the number of transducers required for bringing liquids together.

For Claim 22, Wixforth does not teach a second constriction at the analysis point. It would have been obvious to one of ordinary skill in the art at the time of invention to use such constriction since so doing applies the same physical principles already used in the teachings of Wixforth on confinement of liquid to and directional movement from a reservoir, surface tension and control of surface wetting properties.

For Claim 23, Wixforth is silent on moving the reservoir drop to and fro. Wixforth does teach that at least two acoustic waves can be used to establish the direction of matter and that the region 13 may have a coating to accelerate a reaction [0079]. It would have been obvious to one of ordinary skill in the art from these teachings to move a drop back and forth across a region (for analysis), in order to obtain sequential and separate exposure to analysis and reaction regions, thereby obviating the effect of exposure of light from an analysis region to reagents that may be coated on the reaction region.

Conclusion

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY G. KINGAN whose telephone number is (571)270-3720. The examiner can normally be reached on Monday-Friday, 8:30 A.M. to 5:00 P.M., E.S.T..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on 571 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TGK

/Jill Warden/
Supervisory Patent Examiner, Art Unit 1797